

Application No.: 09/234,028  
Response dated: July 12, 2007  
Reply to Office Action dated: January 12, 2007

## REMARKS

By a non-final Office Action dated January 12, 2007, the Examiner in charge of this application rejected the claims under 35 U.S.C. §§ 112 and 102. Applicant responds to each of the Examiner's rejections below. In view of the amendments noted above and the remarks presented herein, applicant respectfully requests reconsideration of the merits of this application.

### Claim Rejections - 35 U.S.C. § 112

The Examiner rejected Claims 1-7 under 35 U.S.C. § 112, second paragraph, as being indefinite. The Examiner alleged that the phrase "only by having at least one amino acid substitution" is unclear. Applicant amends Claim 1 to delete the word "only" from the phrase. As such, this rejection as applied to Claims 1-7 is now moot.

The Examiner then rejected Claims 1-7, 9-10 and 15 under 35 U.S.C. § 112, first paragraph, for failing to comply with the written description requirement. The Examiner alleged that the specification does not contain an adequate description for a broad genus of claims that includes any and all modified ribonuclease inhibitors. In addition, the Examiner alleged that the specification does not describe additional species by sufficient structural characteristics other than those recited in Claim 1. Applicant disagree with the rejection.

However, to expedite prosecution on the merits, applicant amends Claim 1 to clarify that the structure of the native ribonuclease inhibitor (RI) is defined by SEQ ID NOS: 2 and 3. Applicant amends Claims 2, 9 and 15 to recite the structural limitation of SEQ ID NO:3. Also, applicant adds new Claim 17 mirroring Claim 2, but defining the structure of the native RI to be porcine, SEQ ID NO:2. In view of these amendments, applicant respectfully requests reconsideration of this rejection as applied to Claims 1-7, 9-10 and 15.

The Examiner then rejected Claims 1-7, 9-10 and 15 under 35 U.S.C. § 112, first paragraph, for failing to meet the enablement requirement. The Examiner alleged that the specification does not reasonably provide enablement for any variant ribonuclease inhibitor having at least one amino acid substitution in at least one of its adjacent cysteine residues to an amino acid residue not capable of forming a disulfide bond, the mutant ribonuclease inhibitor retaining its specificity and binding affinity to ribonuclease. As noted above, applicant amends Claims 1-2, 9 and 15 to recite additional structural requirements (i.e., limit

Application No.: 09/234,028  
Response dated: July 12, 2007  
Reply to Office Action dated: January 12, 2007

the native RI to SEQ ID NOS:2 and 3) supported by the application. The Examiner acknowledged that the specification is enabled for SEQ ID NO:3. Applicant submits that the specification is also enabled for SEQ ID NO:2, which shows an adjacent pair of cysteine residues at 324 and 325, which is reflected in new Claim 17. Other inconsequential amendments were made to Claim 1 for clarification purposes only. Support for the amendments is found for example, at page 7, lines 24-35 of the specification. No new matter has been introduced into the claims. In view of these amendments, applicant respectfully requests reconsideration of this rejection as applied to Claims 1-7, 9-10 and 15.

Claims Rejections - 35 U.S.C. § 102

The Examiner rejected Claims 1-7, 9, 10 and 15 under 35 U.S.C. § 102(b) as anticipated by Blázquez M, *et al.*, "Oxidation of sulphydryl groups of ribonuclease inhibitor in epithelial cells is sufficient for its intracellular degradation," *J. Biol. Chem.* 271:18638-18642 (1996). The Examiner alleged that Blázquez *et al.* anticipate the pending claims by disclosing a human ribonuclease inhibitor having at least one amino acid substitution in at least one of two adjacent cysteine residues, the substitution being to an amino acid not capable of forming a disulfide bond with the adjacent residue. Applicant respectfully disagrees.

Blázquez *et al.* does not disclose human RI. It also does not relate to a modified RI having at least one amino acid substitution in at least one of two adjacent cysteine residues in the amino acid sequence of the native RI. Instead, Blázquez *et al.* relates to porcine RI. *See* p. 18638, abstract and first full paragraph. In addition, Blázquez *et al.* do not disclose any amino acid substitutions. Blázquez *et al.* only showed that cysteine residues of porcine RI can be oxidized intracellularly, which caused inactivation and disappearance of the RI from cells. *See* abstract. This is not the same as an amino acid substitution -- Blázquez *et al.* made no structural alteration to porcine RI. As such, Blázquez *et al.* does not anticipate the pending claims. In view of these remarks and the amendments noted above, applicant respectfully requests reconsideration of this rejection as applied to Claims 1-7, 9, 10 and 15.

The Examiner further rejected Claim 16 under 35 U.S.C. § 102(b) as anticipated by Lee F, *et al.*, "Primary structure of human placental ribonuclease inhibitor," *Biochemistry* 27:8545-8553 (1988). The Examiner alleged that Lee *et al.* anticipate the pending claim by

Application No.: 09/234,028  
Response dated: July 12, 2007  
Reply to Office Action dated: January 12, 2007

disclosing methods of isolating and the primary structure of human RI having a structure of SEQ ID NO:3. Applicant respectfully disagrees.

To expedite prosecution on the merits, applicant amends Claim 16 to recite that the variant has an amino acid substitution in at least one of two adjacent cysteine residues, and that the substitution is an alanine for a cysteine. Support for this amendment is located on p. 7, lines 23-27 of the application. Lee *et al.* does not disclose a human RI variant having such a structure. Thus, Lee et al. does not anticipate Claim 16.

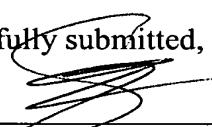
Applicant has made a diligent effort to place the claims in condition for allowance. However, should there remain unresolved issues that require adverse action, it is respectfully requested that the Examiner telephone applicant's attorney at the number listed below so that such issues may be resolved as expeditiously as possible.

For the reasons stated above, and in view of the above amendments, this application is now considered to be in condition for allowance and such action is earnestly solicited.

Fees

A petition for a three-month extension of time accompanies this response so that it will be deemed to have been timely filed. No other extension of time is believed due, but should any additional extension be due, in this or any subsequent response, please consider this to be a petition for the appropriate extension and a request to charge the extension fee to Deposit Account No. 17-0055. No additional fees are believed due; however, if any fees are due, in this or any subsequent response, please charge Deposit Account 17-0055.

Respectfully submitted,

  
Sara D. Vinarov  
Reg. No.: 48,524  
Attorney for Applicant  
QUARLES & BRADY LLP  
P.O. Box 2113  
Madison, WI 53701

TEL 608/251-5000  
FAX 608/251-9166